

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

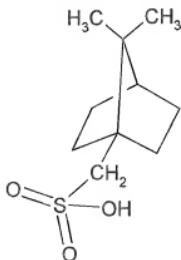
Appln. Of:	GEORGE KRSEK)	
Serial No.:	10/772,675)	
Filed:	February 4, 2004)	
For:	METHOD TO SEPARATE STEREOISOMERS)	
Group:	1723)	
Examiner:	DRODGE, JOSEPH	DOCKET: KONEC 04.01)

Commissioner of Patents & Trademarks
Washington, D.C. 20231

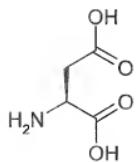
DECLARATION UNDER 37 CFR 1.132

I, GEORGE R. KRSEK, Ph.D., hereby declare:

1. I am an Applicant in the above-referenced Application.
2. I prepared and/or purchased a variety of optically active acids, and attempted to use each of those optically active acids to resolve dl-methylphenidate.
3. Between July 9, 2001 and July 23, 2001, I unsuccessfully attempted to resolve dl-threo-methylphenidate using d-10-camphor sulfonic acid, compound I,

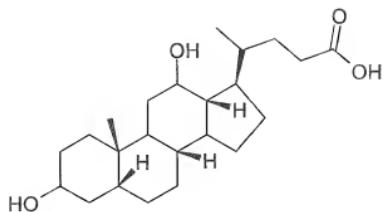


L-aspartic acid, compound II,



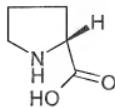
II

Deoxycholic acid, compound III



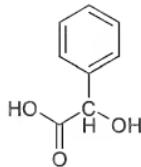
III

D-pyrrolidine carboxylic acid, compound IV,



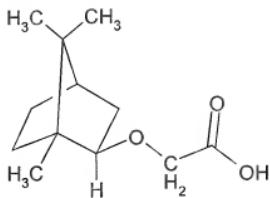
IV

and (+) Mandelic acid, compound V



V

4. On September 10, 2001, I attempted without success to resolve dl-threo-methylphenidate using (-) borneoloxoacetic acid, compound VI



VI

5. Attachment "A" hereto recites data relating to the synthetic yield reported by Leffler and Calkins ("Leffler") for the preparation of *l*-menthoxyacetic acid from *l*-menthol, and data reported in the Application on Page 9 / Line 16 through Page 10 / Line 20 for my preparation of *l*-fenchyloxyacetic acid from *l*-fenchyl alcohol.

6. Attachment "B" hereto comprises true and accurate copies of Page 1188 and Page 1513 of the 2005-2006 Aldrich Catalog ("Aldrich").

7. Aldrich at Page 1188 recites a price for optically *l*-fenchyl alcohol of \$62.90 for 500 grams. See, Attachment "B" at Page 1188 - Product No. 196444-500G.

8. Aldrich at Page 1513 recites a price for *l*- menthol of \$94.50 for 500 grams.

See, Attachment "B" at Page 1513 - Product No. M2780-500G-A.

9. Leffler reports a yield of 78-84% for the synthesis of *l*-menthoxyacetic acid from *l*-menthol. See, Leffler at Page 2.

10. I prepared 90 grams, or 0.48 moles, of *l*-fenchyloxyacetic acid using 200 grams, or 1.30 moles, of *l*-fenchyl alcohol for a yield of 36.90%. See, Application at Page 9 / Line 16 through Page 10 / Line 20.

11. Using the yield reported by Leffler and starting with 500 grams of *l*-menthol would give 475 grams of *l*-menthoxyacetic acid.

12. The price of *l*- menthoxyacetic acid produced, based on the cost of the starting *l*-menthol, would be \$0.20 per gram.

13. Using the method of Example4 of the Application and starting with 500 grams of *l*-fenchyl alcohol would give 225 grams of *l*-fenchyloxyacetic acid.

14. The price of *l*-fenchyloxyacetic acid produced, based on the cost of the starting *l*-fenchyl alcohol, would be \$0.28 per gram.

15. The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.


GEORGE R. KRSEK, Ph.D.

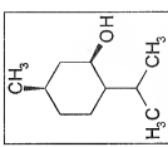
Date: 1 Nov 06

CERTIFICATE OF ELECTRONIC FILING

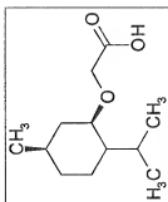
I hereby certify that on this 2nd day of November, 2006, the Declaration Under 37 CFR 1.132 is being filed via the Web Enabled Patent Filing System (EFT-WEB).

By: 

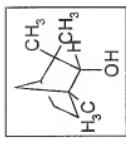
ATTACHMENT “A”



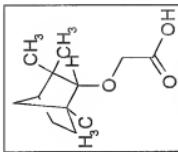
MENTHYL ALCOHOL
MOL. WT. = 156 g/mole



FENCYL ALCOHOL
MOL. WT. = 154 g/mole



MENTHOXYACETIC ACID
MOL. WT. = 190 g/mole



FENCOXYACETIC ACID
MOL. WT. = 188 g/mole

STARTING ALCOHOL	PRICE FOR 500 G STARTING ALCOHOL	YIELD FOR OPTICALLY ACTIVE OXYACETIC ACID FROM STARTING ALCOHOL	YIELD IN GRAMS OF OPTICALLY ACTIVE OXYACETIC ACID STARTING WITH 500 G. ALCOHOL	PRICE PER GRAM BASED ON STARTING ALCOHOL
MENTHOL	\$94.50	78%	475 grams	\$0.20
FENCYL ALCOHOL	\$62.90	36.80%	225 grams	\$0.28

ATTACHMENT “B”

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■ Fatbrownrr ■

Fat Brown RR

[6416-57-5]	C11H28S	C ₁₁ H ₂₈ S ₄	FW 262.31
Dye content	95%		
mp	147 to 158 °C		
λ _{max}	451 nm		
R. 36/37/38 S. 26-36 RTECS# ST2900030 TSCA			
236039-25G	glass btl 25 g	31.00	

Fatty acid methyl esters/C₁₀-C₂₄, straight-chain, kit containing 19 standards

25,222-0 Methyl arachidate 1g			
85,527-2 Methyl behenate 500mg			
25,600-2 Methyl caprate 5mL			
26,067-3 Methyl caprylate 2.5g			
29,903-0 Methyl decanoate 2.5g			
14,900-4 Methyl enanthate 2.5mL			
28,607-9 Methyl heptadecanoate 250mg			
29,904-9 Methyl hexadecanoate 100mg			
23,459-1 Methyl laurate 2.5g			
14,898-9 Methyl myristate 2.5g			
28,683-4 Methyl nonadecanoate 500mg			
24,589-5 Methyl nonanoate 2.5g			
26,089-7 Methyl palmitate 1g			
23,549-3 Methyl pentadecanoate 2.5g			
58,070-9 Methyl stearate 1g			
29,905-7 Methyl tetradecanoate 100mg			
28,734-2 Methyl tricosanoate 100mg			
MR.540-9 Methyl tridecanoate 2.5g			
29,941-3 Methyl undecanoate 2.5g			
29902-1KT	1 kit	400.80	

Fatty acids/C₁₀-C₂₄, straight-chain, kit containing 19 standards

E23-1 Arachidic acid			
21,694-1 Behenic acid			
15,376-1 Decanoic acid			
15,378-8 Dodecanoic acid			
21,966-5 Hexadecanoic acid			
H100-0 Heptadecanoic acid			
25,873-7 Heptanoic acid			
13,345-5 Hexanoic acid			
15,379-6 Myristic acid			
N5252 Nonadecanoic acid			
N2,990-2 Nonanoic acid			
15,375-3 Octanoic acid			
25,872-3 Palmitic acid			
P360-0 Pentadecanoic acid			
26,838-0 Stearic acid			
23,468-0 Tetraacosanoic acid			
21,859-6 Tricosanoic acid			
T0502 Tridecanoic acid			
17,147-6 Undecanoic acid			
— R. 34 S. 26-28/36/37/39/45			
298514-1KT	1 kit	286.20	

Fenbuten, 96%

[36330-85-5]	C ₁₂ H ₂₂ C ₆ H ₅ COCH ₂ Cl ₂ CO ₂ H	C ₁₂ H ₂₂ C ₆ H ₅ COCH ₂ Cl ₂ CO ₂ H	FW 254.28
Merck 13,3990			
mp	184 to 187 °C		
R. 29 S. 26-45 RTECS# DV1761000			
538515-1G	glass btl 1 g	21.90	
538515-5G	glass btl 5 g	72.90	

538515-1G	glass btl 1 g	21.90	
538515-5G	glass btl 5 g	72.90	

(1R)-(-)-Fenchone, -98%

(-)-Fenchone, (-)-1,3,3-Trimethyl-2-norbornanone			
7787-20-4	C ₁₀ H ₁₆ O	FW 152.23	
bp.	50-55°, neat		
bp.	71V/212, Fleiss 8,228		
bp.		192-194 °C	
density	0.948 g/mL 25 °C		
mp	5 to 6 °C		
n _D ²⁰	1.461		
R. 10 S. 23-24/25; TSCA Fp. 52°C (128°)			

196436-50G

glass btl 50 g

23.30

196436-25G

glass btl 250 g

73.30

(+)-Fenchone, >98.0% (GC, sum of enantiomers)

(1S)-1,3,3-Trimethylbicyclo[2.2.1]heptan-2-one, (+)-1,3-Tri-

methyl-2-norbornanone

[4695-62-9] C₁₀H₁₆O FW 152.23

purum

otf[®] +60.3°, neat

Merck 13,3995, Bell. 7IV,212

bp.

63-65 °C/13 mm Hg mp

5 to 7 °C

density

0.945 g/mL 20 °C

mp

5 to 6 °C n_D²⁰

1.463

S. 23-24/25 RTECS# R87875200 Fp. 66°C (151°)

46210-100ML-F

100 mL

115.10

S. 22-24/25 Fp. 74°C (165°)

39 to 45 °C

S. 22-24/25 Fp. 74°C (165°)

5 to 7 °C

196444-45G

glass btl 5 g

18.90

196444-100G

glass btl 100 g

20.30

196444-500G

glass btl 500 g

62.90

Fenoxazop ethyl, see Ethyl (25-4)-2-(4-(6-chlorobenzoyl)-2-

phenyl)-2-hydroxypropionate Page 1128

Fenoxazone, see 3-(2-phenyl-5,6-bis(4-alkoxy-2-furyl)-1,2,4-triazine dioxin

salt Page 1128

Feric ammonium citrate, see Ammonium iron(III) citrate Page 224

Feric citrate

Fe(OH)₃, see Iron(III) hydroxide Page 1128

Fe(OH)₃

16-18.5%

Light sensitive

F6129-250G

250 g

30.60

F6129-1KG

1 kg

100.20

Feric hydroxide oxide

[20344-49-4] Fe(OH)₃ FW 88.85

Merck 13,4055

TSCA

crystalline powder, 50-80 mesh

546267-50G

poly btl 50 g

45.70

546267-250G

poly btl 250 g

170.00

catalyst grade, 30-50 mesh

371254-50G

poly btl 50 g

47.00

371254-250G

poly btl 250 g

178.50



retroene

[102-54-5]

Merck 13,4C

bp.

λ_{max}

0.2X

F408-11

F408-100G

Ferronoxine

[1287-16-7]

Bell. 16,V,1

mp

X 202

330-045-50X

Leroneose

[1316-91-2]

Bell. 16,V,1

mp

X 202

335-053-1G

335053-SG

retroene

[12152-94-2]

Contains vir

mp

R. 3637

455547-SG

455547-ZSG

retroene

[1271-42-7]

Bell. 16,V,1

mp

106887-1G

106887-10E

1,1'-Fericose

C₂₂H₂₂O₂

mp

S 22-24/25

1,1'-Fericose

C₂₂H₂₂O₂

mp

163750-10

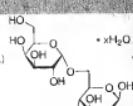
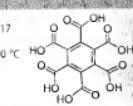
163750-10G

1,1'-Fericose

[1271-48-3]

mp

496391-500I

US \$		US \$		■ Menthylacetate ■	
	+ xH ₂ O				
dec.)					
5 g	34.00				
10 g	59.10				
25 g	117.50				
100 g	295.50				
PW 452.80					
92 to 94 °C					
glass btl 100 mg	37.10				
glass btl 1 g	264.50				
42.17					
~300 °C					
	-				
glass btl 1 g	39.90				
to 300 °C, kit containing 24					
34-136°C					
286°C					
1°C					
10 190-200°C					
dinitrophenylhydrazone 159-					
methylenephthalimide 70-73°C					
40 241°C					
area 59.61°C					
and 209-210°C					
21°C					
128-130°C					
and 270-272°C					
and 248-252°C					
9-26°C					
86°C					
70-172°C					
glutaric acid 180-181°C					
133°C					
concoct and 219-220°C					
150-152°C					
1 kit	290.40				
					
atom % D)					
K&T Dept demonstration					
R 22-38-41/48/2022 S 36/37/39 Hygroscopic					
551376-1EA	5mm x 8in. 1ea	116.00			
					
LC-NMR reference standard, 50% in chloroform-d (99.9					
atom % D), chromium(III) acetylacetone 0.5%					
R 22-38-40-41/48/2022 S 36/37/39 Hygroscopic, light sensitive					
613290-1EA	5mm x 8in. 1ea	318.00			
					
(2Z)-3,5(R)-Menthone					
(2Z)-3,5(R)-C ₁₀ H ₁₆ O	PW 156.27				
Bell 6,150, Fieser 12,294, 13,172, 16,203					
bp	0.89 g/ml, 25 °C				
density	0.89 g/ml, 25 °C				
mp	41-44 °C				
vp	42 to 45 mm Hg (20 °C)				
p R 37/8-41 S 26-39 RTECS# O107020000 Fp 101°C (214°F)	CH ₃ HO C ₆ H ₅ OH				
59%					
[α] _D ²⁰ = -50°, c = 10 in C ₂ H ₅ OH					
ee 99% (GLC)					
M2780-25G-A	poly btl 25 g	14.30			
M2780-100G-A	poly btl 100 g	29.20			
M2780-500G-A	poly btl 500 g	94.50			
					
(S)-Menthylacetate, 99% sublimed					
[α] _D ²⁰ = -50°, c = 10 in CH ₃ CH ₂ OH					
TSCA					
588733-1G	glass btl 1 g	34.50			
(R)-Menthylacetate, 99% sublimed					
[α] _D ²⁰ = +48°, c = 10 in C ₂ H ₅ OH					
ee: 96% (GLC)					
Bell 6,151, Fieser 12,294, 13,172					
bp	43 to 44 °C				
vp	0.8 mm Hg (20 °C)				
S 37/8-41 S 26-36 RTECS# O107020000 TSCA					
Fp 101°C (214°F)					
224464-10G	glass btl 10 g	33.30			
224464-50G	glass btl 50 g	110.50			
(S)-Menthine, 50%					
[α] _D ²⁰ = -97.3°, C ₁₀ H ₁₆ O	PW 154.25				
[α] _D ²⁰ = -20°, neat					
Merck 13,5862, Bell 7,IV,87; Fieser 14,201;					
16,204					
bp	207-210 °C				
density	0.893 g/ml, 25 °C				
vp	0.5 mm Hg (20 °C)				
[α] _D ²⁰ = -45					
isomethane		5%			
S 23-24/25, TSCA Fp 72°C (162°F)					
218235-25G	glass btl 25 g	23.60			
218235-100G	glass btl 100 g	54.00			
(S)-Menthylacetyl chloride, 97%					
[α] _D ²⁰ = -62.4°, C ₁₂ H ₂₂ ClO ₂					
Fw 232.75					
[α] _D ²⁰ = -10°, neat					
density	1.033 g/ml, 25 °C				
[α] _D ²⁰ = -1.469					
R 34 S 26-27/37/39/45					
Fp 113°C (235°F)					
453714-1G	glass btl 1 g	23.90			
453714-5G	glass btl 5 g	79.80			
(R)-Menthyl acetate, 97%					
[α] _D ²⁰ = -48.5°, C ₁₂ H ₂₂ O ₂	PW 198.30				
Merck 13,5863, Bell 6,150					
bp	228-229 °C				
[α] _D ²⁰ = -0.922 g/ml, 25 °C					
TSCA Fp 92°C (198°F)					
218230-25M	glass btl 25 ml	21.90			
422770-100ML	glass btl 100 ml	60.70			
(S)-Menthyl acetate, 98%					
[α] _D ²⁰ = -23-26°, C ₁₂ H ₂₂ O ₂	PW 198.30				
[α] _D ²⁰ = -81°, c = 8 in C ₂ H ₆					
ee 98% (GLC)					
Bell 6,151					
bp	229-230 °C				
[α] _D ²⁰ = -0.92 g/ml, 25 °C					
RTECS# AB9000000, TSCA Fp 77°C (171°F)					
441058-25ML	glass btl 25 ml	24.60			
441058-100ML	glass btl 100 ml	65.60			